

## Coronary revascularization in stable coronary artery disease: the new European Society of Cardiology Guidelines on chronic coronary artery disease

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The targets of treatment in patients with stable coronary artery disease (SCAD), are symptoms relief, delay or prevent complications such as death, heart failure, or myocardial infarction (MI), maintain quality of life of these patients and at the end minimize health care costs. The 2006 ESC guidelines encouraged coronary angiography and revascularization as the initial management strategy for patients with SCAD<sup>1</sup>. So what has changed and what is new in the new 2013 ESC guidelines<sup>2</sup>?

The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial<sup>3</sup> had a major impact on clinical decision making and guidelines implementation. The trial showed that although percutaneous coronary intervention (PCI) reduces ischemic burden more rapidly than does optimal medical therapy (OMT), medical therapy may achieve a comparable reduction in angina in the long run. In COURAGE, 2287 patients with SCAD and significant stenosis in at least one proximal epicardial coronary artery, were randomly assigned to either OMT alone or OMT and PCI. At a median follow-up of 4.6 years, PCI did not reduced long-term rates of mortality and non-fatal MI (HR: 1.05; 95%CI: 0.87 -1.27), nor complications such as hospitalization for acute coronary syndromes (HR: 1.07; 95% CI: 0.84 -1.37). Later, there were some post hoc observational studies that were dissonant with the main findings of COURAGE. Some analyses<sup>4</sup> suggested that baseline myocardial ischemia (>10% on stress myocardial perfusion scintigraphy) may be most important in those with more severe atherosclerotic burden that, in turn, may benefit more from PCI. This provides an important justification for the ongoing ISCHEMIA trial which is using Coronary Computed Tomography Angiography (CCTA) to exclude patients with minimal atherosclerotic disease. Other analyses are discordant with such studies implying that the severity of ischemia itself cannot identify patients who would benefit from an invasive strategy, and suggest that among patients with stable ischemic heart disease, baseline assessment of anatomic burden predicts future events<sup>5</sup>.

The quality of information on guidelines cannot rely upon one trial and its post-hoc analyses. Two other trials deserve to be mentioned: The Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D)<sup>6</sup> and the Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2 (FAME-2)<sup>7</sup> trials. The BARI 2D trial<sup>6</sup> evaluated 2368 patients with SCAD and type-2 diabetes mellitus. Patients were randomly assigned to undergo either revascularization or OMT. Yet revascularization failed to significantly reduce, both the 5-years mortality rates (11.7% versus 12.2%, p=0.97) and the combined endpoint of major cardiovascular events (22.8% versus 24.1%, p=0.70). Data are therefore suggesting that the overlapping anti-ischemic nature of both strategies may contribute over the long term to the abrogation of the prognostic importance of baseline, pretreatment inducible ischemia. On the other hand, the FAME-2<sup>7</sup> demonstrated that ignoring the anatomy can sometimes be dangerous. The FAME-2 trial enrolled 888 patients with at least one stenosis with an Fractional Flow Reserve (FFR) of 0.80 or less in an epicardial artery, and compared PCI guided by FFR plus OMT versus OMT alone. PCI guided by FFR significantly reduced the 2-year primary combined endpoint of death and MI (HR: 0.32; 95% CI: 0.19- 0.53) and the secondary endpoint of urgent revascularization (HR: 0.13; 95%CI: 0.06-0.30).

How can these above mentioned studies reconcile and translate into recommendations for clinical decision making? First of all, we have called attention to the clinical consequences of misinterpretation of the COURAGE and BARI 2D trial results. These studies mandated pre-randomized catheterization specifically to exclude patients with high-risk anatomy who would necessarily get revascularization. Guidelines have interpreted the COURAGE by implying that physicians do not have to catheterize patients if they are at low or intermediate risk using non invasive assessment, because revascularization is not going to make a difference in this population. Importantly, guidelines recommend that baseline CCTA will provide a crucial opportunity to evaluate the prognostic importance of the anatomic burden of disease, and physicians may learn whether anatomy trumps ischemia in this higher-risk group. Guidelines, furthermore, recommend some physiopathological criteria for definition of the relevance of coronary anatomy. FFR is deemed to give the best information. FFR is especially indicated for the identification of functional stenosis severity of patients in whom stress tests are contraindicated or are inconclusive. Of course, revascularization is reserved for patients with refractory angina despite optimal medical therapy. As well, OMT is the first approach and all patients with SCAD should receive it<sup>8</sup>.

### LITERATURE

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